DADMAC HPV COMMITTEE
FINAL US HPV CHALLENGE SUBMISSION
DIALLYLDIMETHYLAMMONIUM CHLORIDE (CAS NO. 7398-69-8)

November 15, 2006

The DADMAC HPV Committee is providing this information as a follow-up to its November 22, 2005 response to EPA's July 21, 2005 comments on the Committee's HPV submission for diallyldimethylammonium chloride (CAS No. 7398-69-8) from April 2004. With this response, the sponsor (DADMAC HPV Committee) considers its HPV commitment complete for this substance.

(1) ***Ecological Effects Testing (fish, invertebrates, and algae)***

EPA comment, July 21, 2005: EPA agrees with the submitter's proposal to test for these endpoints according to OECD TG's 203, 202, and 201, respectively.

Committee response, November 22, 2005: The DADMAC HPV Committee is currently exploring conducting studies regarding ecological effects as noted in the original test plan submission. The industry is further exploring whether these studies might be available through producers in other parts of the world. At the same time, the Committee has begun to question the appropriateness of conducting additional aquatic toxicity tests in light of the existing data on this material (already provided as part of the initial robust summary submission), as well as the information attached from the EPA PBT profiler (Attachment I); which estimated DADMAC was "not chronically toxic to fish." A decision will be made in the near future and the Committee will notify EPA at that time.

Committee response, November 15, 2006: The DADMAC HPV Committee embarked on a review of the available data on potential ecological effects and also considered possible testing approaches, including considerations of goals to minimize live animal testing. Based on the review, at this time, it does not appear that additional testing is warranted. The Committee will inform the Agency of any changes in this position.

(2) ***Repeated-Dose Toxicity – Updated Summary***

EPA comment, July 21, 2005: A 13-week repeated-dose toxicity study in dogs omitted details of clinical observations, whether or not ophthalmological examination was performed, frequency of weight measurements, effect on food consumption, hematology and clinical chemistry parameters evaluated, organs weighed at necropsy and organs examined histopathologically.

Committee response, November 22, 2005: A revised robust summary is being prepared and will be submitted in the coming weeks.

Committee response, November 15, 2006: A revised summary is on the following page.

5.4 REPEATED DOSE TOXICITY

Type	:	13-week oral toxicity feeding study
Reference	:	Tegeris, A. (1976)
Species	:	dog
Sex	:	male and female
Strain	:	beagle
Route of admin.	:	Oral, feed
Exposure period	:	90 days
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	50, 200, 800 mg/kg/day
Control group	:	yes, concurrent, no treatment
NOAEL	:	= 200 mg/kg/day
LOAEL	:	= 800 mg/kg/day
Method	:	Groups of 4 male and 4 female purebred beagle dogs, averaging 3 to 4 months old, were fed diets containing 50, 200, or 800 mg/kg/day of DADMAC monomer. Diets were adjusted to deliver specified doses of monomer in a 350 gram meal. The dogs were carefully observed for 13 weeks. Samples were taken for clinical chemistry and hematology at 45 days and at termination. All dogs were necropsied and histopathology performed. Ophthalmological examination performed biweekly. Measurements of weight conducted monthly; weekly for effect on food consumption; and, monthly for hematology and evaluation of clinical chemistry parameters. Organs weighed at necropsy: heart, liver, brain, spleen, kidneys (left and right), adrenals (left and right), prostate, uterus and lung. Organs examined histopathologically (monthly): liver, kidneys, urinary bladder, bone marrow, spleen, lymph node, pancreas, stomach, large intestine, small intestine (2), thyroid (2), adrenals (2), pituitary, trachea and esophagus.
Result	:	At 800 mg/kg/day, there was a decrease in body weight gain. Otherwise there were no treatment related effects in this study. The NOAEL was 200 mg/kg/day.
Test substance	:	DADMAC (45% solution in water)
Conclusion	:	The NOAEL for this study is 200 mg/kg/day.
Reliability	:	(1) valid without restrictions. Guideline study.
Test substance	:	DADMAC (45% solution in water)
Reference	:	(11) Tegeris, A. (1976). DADM: Ninety Day Feeding to Dogs. Pharmacopathics Research Laboratories, Laurel, MD.